```
=> s adenovirus and (E2F) (5A) promoter
L1         223 ADENOVIRUS AND (E2F) (5A) PROMOTER

=> s adenovirus and (E2F) (3A) promoter
L2         196 ADENOVIRUS AND (E2F) (3A) PROMOTER

=> s adenovirus and (E2F) (3A) promoter (S) (termination or insulator or polya or polyadenylation)
L3           2 ADENOVIRUS AND (E2F) (3A) PROMOTER (S) (TERMINATION OR INSULATOR
                OR POLYA OR POLYADENYLATION)

=> d ibib abs 1-2

L3   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2002:676177  CAPLUS
DOCUMENT NUMBER:          137:211937
TITLE:                    Construction of adenoviral vectors containing
                          insulating sequence for minimization of leaky
                          therapeutic gene expression
INVENTOR(S):              Gorziglia, Mario; Hallenbeck, Paul L.; Kaleko,
                          Michael; Clarke, Lori; Phipps, Sandrina; Jakubczak,
                          John Leonard
PATENT ASSIGNEE(S):       Novartis A.-G., Switz.
SOURCE:                   PCT Int. Appl., 41 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002068627      A2   20020906       WO 2002-US5280   20020222
     WO 2002068627      A3   20030612
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
             UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2003104624      A1   20030605       US 2002-81961    20020222
PRIORITY APPLN. INFO.:                     US 2001-270985P  P  20010223
AB   The present invention relates to adenoviral vectors and their use in
     methods of gene therapy.  The present invention provides novel viral
     vectors and methods useful for the minimization of leaky gene expression,
     and, in particular, of nonspecific transcriptional read-through of genes.
     Such constructs may be obtained by the insertion of an insulating sequence
     into a vector construct, such as for example a termination signal sequence
     upstream of the transcription initiation site of the resp. transcription
     unit.  Provided is a recombinant viral vector comprising an adenoviral
     nucleic acid backbone, wherein said nucleic acid backbone comprises in
     sequential order: a left ITR, a termination signal sequence, an
     E2F-1 promoter which is operably linked to a gene
     essential for replication of the recombinant viral vector, an adenoviral
     packaging signal, and a right ITR.

L3   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2002:675779  CAPLUS
DOCUMENT NUMBER:          137:210924
TITLE:                    Oncolytic adenoviral vectors expressing therapeutic
                          genes for the treatment of cancer
INVENTOR(S):              Ennist, David Leonard; Forry-Schaudies, Suzanne;
                          Gorziglia, Mario; Hallenbeck, Paul L.; Hay, Carl M.;
                          Jakubczak, John Leonard; Kaleko, Michael; Ryan,
                          Patricia Clara; Stewart, David A.; Xie, Yuefeng;
                          Connelly, Sheila; Police, Sehidhar Reddy; Clarke,
                          Lori; Phipps, Sandrina; Cheng, Cheng
PATENT ASSIGNEE(S):       Novartis Pharma A.-G., Switz.
SOURCE:                   PCT Int. Appl., 226 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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WO 2002067861 A2 20020906 WO 2002-US5300 20020222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003104625 A1 20030605 US 2002-81969 20020222
PRIORITY APPLN. INFO.: US 2001-270922P P 20010223
US 2001-295037P P 20010601
US 2002-348670P P 20020114

AB The present invention relates to oncolytic adenoviral vectors and their use in methods of gene therapy. Provided is a recombinant viral vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises in sequential order: a left ITR, a **termination** signal sequence, an **E2F** responsive **promoter** which is operably linked to a gene essential for replication of the recombinant viral vector, an adenoviral packaging signal, and a right ITR. The adenoviral vectors may also comprise a polynucleotide encoding a cytokine such as GM-CSF that can stimulate a systemic immune response against tumor cells. The preferred vector Ar6pAE2fF comprises an **adenovirus** vector that uses a fragment of the human E2F-1 promoter to selectively regulate E1A expression and thus adenoviral replication in tumor cells. Ar6pAE2fF selectively kills Rb-pathway defective tumor cells over normal primary cells, and is preferentially replicated in human tumor cell lines vs. normal primary cells. This vector has a superior early toxicity profile to the non-selective replication competent virus, Addl327, when administered i.v. in SCID mice and provides advantages in efficacy, selectivity, and safety as compared to the oncolytic viral vector Addl1520. Ar17pAE2fTrtex is a particularly preferred, tumor-selective oncolytic **adenovirus** designed for the treatment of a broad range of cancer indications involving the two most common alterations in human cancer, namely defects in the Rb-pathway and overexpression of telomerase. Ar17pAE2fTrtex utilizes a E2F-1 promoter to control expression of the adenoviral E1A gene and the adenoviral E4 gene is controlled by a hTERT (human telomerase reverse transcriptase) promoter. Ar17pAE2fTrtex is expected to replicate in the majority of cancer cells, lead to tumor selective expression of toxic viral proteins, cytolysis, and enhancement of sensitivity to chemotherapy, cytokines, and cytotoxic T lymphocytes.

FILE 'MEDLINE, CAPLUS' ENTERED AT 08:19:17 ON 03 SEP 2003

L1 6 S ITR (10A) (POLYADENYLATION OR POLYA OR POLY (A) ADENYLATION)
L2 4 S (HETEROLOGOUS OR CMV) (A) PROMOTER (10A) (POLYADENYLATION OR
L3 10 S (HETEROLOGOUS OR CMV) (A) PROMOTER (10A) (POLYADENYLATION OR
L4 6 S L3 NOT L2
L5 6 DUP REM L4 (0 DUPLICATES REMOVED)
L6 7 S ITR (5A) (TERMINATION OR POLYADENYLATION OR POLYA)
L7 6 S L6 NOT L4
L8 6 S L7 NOT L3
L9 5 DUP REM L8 (1 DUPLICATE REMOVED)